Serum Prolactin Levels in Homosexual and Bisexual Men With HIV Infection

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Objective: Prolactin is a neurohormone that may be secreted in response to stress and also has regulatory effects on the immune system. Some, but not all, studies suggest that prolactin levels are higher than normal in persons with HIV infection. The authors measured prolactin levels in HIV-positive and HIV-negative homosexual and bisexual men to assess possible differences in levels and then examined relationships between prolactin level and measures of medical status, anxiety, depression, stress, and neuropsychological test performance. Method: Blood for prolactin level determination was obtained from 121 HIV-seropositive and 79 HIV-seronegative homosexual and bisexual men enrolled in a longitudinal study. The men also underwent a daylong assessment that included medical, immunological, psychiatric, psychosocial, psychosexual, and neuropsychological evaluations. Results: There was no statistically significant difference in serum prolactin level among the seronegative men, the seropositive men with no or minimal physical symptoms, and the seropositive men with significant physical symptoms of HIV infection. Furthermore, within the HIV-seropositive group, the correlations between serum prolactin level and measures of depression, anxiety, stress, and neuropsychological test performance were all nonsignificant. Conclusions: Serum prolactin level does not seem to respond to HIV infection or to be related to stress or psychiatric symptoms in HIV-infected men. As none of the subjects had AIDS, the possibility cannot be ruled out that prolactin level increases in very late stages of HIV infection.


The human immunodeficiency virus (HIV) produces disruption in almost every aspect of immune function, ultimately leading to an inability to contain opportunistic infection and neoplastic cell growth. It is clear, however, that a variety of responses are mounted against HIV by the infected host and, at least in early stages, contain the virus’s ability to create immunological collapse. Neuroendocrine factors are known to have a role in regulating immune function, and recent work has examined possible ways in which the hypothalamus and pituitary gland may respond to HIV infection.

Prolactin is one hormone of particular interest because it is believed to have significant interaction with immune function (1–4) and may also be released during stress (5–8). High prolactin levels have also been implicated in panic disorder (9), psychosis (10), and alcoholism with psychosis (11). In all cases, the differences in prolactin level are modest.

A few studies have examined prolactin levels in patients with HIV infection. Croxson et al. (12) measured the prolactin levels of 85 homosexual men. The mean prolactin levels of patients with AIDS and patients with AIDS-related complex were significantly higher than that of seronegative men. The difference in prolactin level between asymptomatic HIV-positive and HIV-negative men was not significant. Nelson et al. (13) also found a higher mean prolactin level in a group of 48 HIV-infected men than in either a group of 13 HIV-negative homosexual men or a group of 14 men described by them as “normal heterosexuals.” Three small studies (14–16) showed no relationship between prolactin level and HIV infection.

The literature therefore suggests that prolactin level may increase with increasing severity of HIV infection, and there are theoretical reasons to believe that prolac-
tinent level may increase with stress or psychiatric illness and play a role in immune function. As part of a longitudinal, multidisciplinary study of patients with HIV infection, we obtained blood for prolactin level determination from HIV-seropositive and HIV-seronegative homosexual and bisexual men during a baseline evaluation that included medical, immunological, psychiatric, psychosexual, and neuropsychological assessments. In our relatively large study group we looked for differences in prolactin level among groups stratified for degree of illness severity. Furthermore, we analyzed the data to determine relationships between prolactin level and measures of illness severity, stress, and psychiatric symptoms.

METHOD

Subjects

The subjects of this report are all enrolled in an ongoing study of HIV infection and are described in more detail elsewhere (17). When the study was initiated in 1988, the cohort of homosexual and bisexual men included 123 HIV-seropositive and 84 HIV-seronegative subjects. One HIV-seropositive subject previously included in the cohort actually had AIDS at the baseline assessment according to information subsequently received and has therefore not been included here. The subjects are seen every 6 months for a daylong evaluation that includes medical history and physical examination, neurological examination, neuropsychological testing, and psychiatric and psychosexual interviews. Blood is obtained for lymphocyte subset analysis, serum p24 antigen level determination, and confirmatory HIV testing. Serum from every subject is then frozen. Occasionally, for technical and scheduling reasons, a blood sample was obtained from a subject later in the day, but no record of this was kept. The nurses responsible for phlebotomy reported that in more than 90% of the cases blood samples from this cohort were obtained in the morning and that any breaches in the protocol occurred at random with respect to the subjects’ HIV status.

Serum prolactin levels were determined from stored frozen serum. The protocol called for blood to be obtained from each subject between 8:30 and 11:00 a.m. Occasionally, for technical and scheduling reasons, a blood sample was obtained from a subject later in the day, but no record of this was kept. The nurses responsible for phlebotomy reported that in more than 90% of the cases blood samples from this cohort were obtained in the morning and that any breaches in the protocol occurred at random with respect to the subjects’ HIV status.

Serum prolactin was measured with double antibody radioimmunoassay (28). The prolactin standard (hPR1-RP-1) and the primary antiserum were donated by the National Pituitary Agency (National Institute of Arthritis, Metabolism and Digestive Diseases). The 125I-labeled PR1 was repurified before use on a G-100 Sephadex column. Anti-rabbit-globulin serum was used to separate the bound and free fractions. The samples were assayed in duplicate. The intra- and interassay coefficients of variance were 6.37% and 6.86% at 3.8 ng/ml, 3.83% and 5.72% at 27.0 ng/ml, and 2.01% and 3.49% at 46.3 ng/ml.

To test for differences in serum prolactin level, we divided the subjects into three groups: HIV seronegative, HIV seropositive with no symptoms or only enlarged lymph nodes (CDC stages II and III), and HIV seropositive with more serious symptoms (CDC stages
TABLE 1. T Cell Concentrations and Test Scores of HIV-Positive and HIV-Negative Homosexual and Bisexual Men

<table>
<thead>
<tr>
<th>Variable</th>
<th>HIV-Positive Men</th>
<th>HIV-Negative Men</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>N</td>
</tr>
<tr>
<td>T cell measure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4*</td>
<td>409.0</td>
<td>222.6</td>
<td>120</td>
</tr>
<tr>
<td>CD8*</td>
<td>829.0</td>
<td>435.3</td>
<td>120</td>
</tr>
<tr>
<td>CD4/CD8 ratio</td>
<td>0.58</td>
<td>0.36</td>
<td>120</td>
</tr>
<tr>
<td>Tests</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hamilton depression scale</td>
<td>4.25</td>
<td>4.16</td>
<td>120</td>
</tr>
<tr>
<td>Hamilton anxiety scale</td>
<td>3.85</td>
<td>3.84</td>
<td>120</td>
</tr>
<tr>
<td>PERI demoralization scale</td>
<td>28.22</td>
<td>14.90</td>
<td>117</td>
</tr>
<tr>
<td>Beck Hopelessness Scale</td>
<td>3.42</td>
<td>4.94</td>
<td>116</td>
</tr>
<tr>
<td>Texas grief inventory</td>
<td>29.33</td>
<td>10.98</td>
<td>108</td>
</tr>
<tr>
<td>Neuropsychologists' impression</td>
<td>0.50</td>
<td>0.67</td>
<td>121</td>
</tr>
</tbody>
</table>

IVa, IVb, IVc-2, and IVe). A three-group analysis of variance (ANOVA) was performed.

To test for a relationship between serum prolactin level and severity of HIV infection, we computed Pearson correlation coefficients within the HIV-positive group for the correlations between prolactin level and both number of CD4+ T lymphocytes and ratio of CD4+ to CD8+ T lymphocytes (CD4/CD8).

To test for a relationship between psychological state and prolactin level, we computed Pearson correlation coefficients for the relationship between prolactin level and scores on the Hamilton depression scale, Hamilton anxiety scale, PERI demoralization scale, Beck Hopelessness Scale, and Texas Revised Inventory of Grief within the HIV-positive group. Finally, we determined the correlation between prolactin level and score on the neuropsychologists' impression within the HIV-seropositive group.

All p values are two-tailed. The number of subjects varies among measures because of missing data.

RESULTS

Table 1 indicates that the HIV-positive patients had significantly fewer CD4+ T cells, significantly more CD8+ T cells, and a significantly lower CD4/CD8 ratio. The HIV-positive subjects had significantly higher demoralization and hopelessness scores and nearly significantly higher anxiety and depression scores than the HIV-negative subjects. The clinical neuropsychological impression and grief scores were not significantly different.

Only six (5%) of the HIV-positive subjects were taking zidovudine at the time of the baseline assessment, and we did not observe any relationship between zidovudine use and prolactin level in this small subgroup. Of other medications taken by the subjects in the study, only the antipsychotic drugs have, to our knowledge, a known effect on prolactin level. However, only two of the 121 HIV-positive men and one of the 79 HIV-negative men were taking these drugs.

Forty-seven (39%) of the seropositive men were in CDC stage II (asymptomatic), 28 (23%) were in CDC stage III (enlarged lymph nodes), and 46 (38%) were in CDC stage IVa, IVb, IVc-2, or IVe. The subjects were divided into three groups: 1) HIV-seronegative, 2) HIV-seropositive—asymptomatic/lymphadenopathy, and 3) HIV-seropositive—symptomatic. Three-group ANOVA of serum prolactin level revealed no significant difference among these groups; the mean levels were 9.2 (SD=3.2), 10.2 (SD=3.4), and 9.9 (SD=3.9) ng/ml, respectively (F=1.47, df=2, 197, p=0.23).

Table 2 indicates that within the HIV-positive group the correlations between serum prolactin level and number of CD4+ T cells, CD4/CD8 ratio, anxiety, depression, demoralization, hopelessness, grief, and neuropsychological performance were all nonsignificant.

DISCUSSION

We did not find higher than normal prolactin levels or a significant correlation between severity of infection and prolactin level in our HIV-seropositive men. Furthermore, we did not observe any relationship between prolactin level and measures of anxiety, depression, or neuropsychological test performance.
Like other groups of subjects (26), our group of HIV-positive subjects was relatively free of psychiatric illness at baseline, and none had AIDS. Without severely anxious, depressed, or medically ill individuals, we may have been limited in our ability to detect a relationship between psychological or medical state and prolactin level.

In an earlier report involving the same subjects (29), we found no significant difference between HIV-positive and HIV-negative homosexual and bisexual men in the level of 24-hour urinary free cortisol. The present findings on prolactin level are similar and, despite the cautions mentioned, suggest that prolactin level, like urinary cortisol level, is not altered in the earlier stages of HIV infection. Nevertheless, it is still conceivable that HIV, because it infects both the immune and the nervous systems, may disrupt normal relationships between neurohormones and immune function, as noted elsewhere (30). Future studies of prolactin’s role in the immune response of HIV-infected patients should focus on more advanced stages of illness, functional measures of immune response (such as mitogen stimulation studies), and patient groups other than homosexual men.

REFERENCES
19. Revision of the CDC surveillance case definition for acquired immunodeficiency syndrome. MMWR 1987; 36(suppl 1):1S–15S

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